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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/400,802	10/21/1999	SUAD EFENDIC	3051-90334	3827

7590 06/04/2003

Eli Lilly and Company
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EXAMINER
GUPTA, ANISH

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/400,802	EFENDIC, SUAD	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6, 7, 16* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

The restriction made in 12-12-00 is hereby withdrawn. All claims have been examined in their entirety.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dietrich et al. in view of Efendic et al. (WO 98/08531) or Efendic (WO98/08873).

The claims are drawn to a method of reducing mortality and morbidity after stroke by the administration of GLP-1 peptide.

Dietrich et al. teach that hyperglycemia can aggregate the consequences of stroke and cerebral ischemia (see abstract). The "hyperglycemic brain ischemia carried out under

normothermic conditions led to acute post-ischemic BBB (blood brain barrier) damage." (See page 115). Further, "[clinical findings indicate that elevated levels of blood glucose are a risk factor for stroke and are associated with a worse prognosis. In a retrospective review of 39 stroke patients, Berger and Hakim concluded that hypyerglycemic patients with serum glucose values greater than 150 mg/dl developed more pronounced cerebral edema and had a worse clinical outcome compared with patients with glucose values less than 100mg/dl." The difference between the prior art and the instant application is that the reference does not teach the administration of GLP-1, GLP-1 analogs and/or derivatives.

However, the references of Efendic teach that GLP-1, GLP-analogs, and GLP-1 derivatives are effective to normalize blood glucose (see abstract in both references). Both references teach that GLP-1 infusion to patients with non-insulin dependent diabetes, was effective in normalizing blood glucose without inducing hypoglycemia (see example 2 in both references).
Both references disclose that a dosage of .25 and 6 pmol/kg/min is effective in normalizing blood glucose levels (see page 24, lines 33-35 of the WO98/08873 and page 20, lines 14-15 of WO98/08531). Note that this is the same concentration as claimed in claim 5 of the instant claims. The references also disclose intravenous, subcutaneously or other parenteral route (see page 18 of the WO 98/08531 and page 21 of the WO 98/08873). Further, the reference disclose the use of GLP-1, GLP-derivatives and GLP analogs within the definition of the terms as disclosed on page 7-15 of the instant specification (see pages 6-11 in WO 98/08531 and pages 7-13 in WO 98/08873). Therefore, it would have been obvious, since increase of glucose levels result worsening of prognosis for stroke and ischemia, and GLP-1 normalizes blood glucose levels, to use GLP-1 or an

analog thereof, to treat stoke and ischemic patients with elevated glucose levels to prevent the worsening of the condition.

1. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dietrich et al. in view of Chen (US 5,512,549).

The claims are drawn to a method of reducing mortality and morbidity after stroke by the administration of GLP-1 peptide.

The reference of Diethrich et al. has been discussed supra. The difference between the prior art and the instant application is that the reference does not teach the administration of GLP-1, GLP-1 analogs and/or derivatives.

Chen et al. disclose the use of GLP-1 (7-37) peptide for the treatment of diabetes (see abstract). The reference discloses that the this analog of GLP -1, has insulinotropic properties (see col. 2, lines 27-30). Hyperglycemic Clamp studies indicated that the GLP-1 analog was effective in controlling levels of glucose and avoid hyperglycemia (see examples 8 and 9 in col. 15-24). The reference teaches that the dosage between 1pg/kg-1000μg/kg, a dosage range within the scope of claimed range (see col. 8, lines 47-50). The reference also discloses various routes of administration, such as parenteral, subcutaneously, and intravenous (see col. 9, lines 14-25 and claims 22-28). Therefore, it would have been obvious, since increase of glucose levels result worsening of prognosis for stroke and ischemia, and GLP-1 normalizes blood glucose levels, to use GLP-1 7-37 or, to treat stoke and ischemic patients with elevated glucose levels to prevent the worsening of the condition.

2. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, can normally be reached on (703)306-3220. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Anish Gupta

Brenda Brumback

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